AMENDED RESPONSE:

Teva USA incorporates its General Objections. Teva USA further objects to this interrogatory to the extent that it calls for the production of information protected from discovery under the attorney-client privilege, the attorney work product doctrine, or any other applicable privilege. Teva USA further objects to this interrogatory as overly broad and unduly burdensome and as seeking information that is neither relevant to any claim or defense in this action nor reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks a response on "each and all of Teva USA's allegations of invalidity of the claims of the patent-in-suit." Teva USA further objects to this interrogatory as seeking information that is neither relevant to any claim or defense in this action nor reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks a response on "each and all of Teva USA's allegations of invalidity of the claims of the patent-in-suit," because Glaxo has not specified which claims it is asserting are infringed. Teva USA also objects to the interrogatory on the grounds that the phrase "the documents reviewed, considered and/or relied on in support thereof" is vague and ambiguous, and, to the extent understood, calls for the disclosure of attorney work product.

Teva USA further objects to this interrogatory as vague and ambiguous to the extent that discovery is in the early stages, and that the Court has not yet construed the claim terms in the asserted claims. Teva USA reserves the right to modify, supplement, and change this response upon further discovery, prosecution of Teva USA's ANDA, and after the Court construes the claims.

Subject to these and the general objections, Teva responds as follows:

United States Patent No. 4,128,658 ("the '658 patent") teaches an oral syrup formulation of ranitidine hydrochloride:

(d) Oral Syrup	% w/v
Active ingredient	2.0
Dilute hydrochloric acid BP, as required	
Sorbitol Solution BPC	60 v/v
Flavour	as required
Distilled water	to 100

'658 patent, col. 29, lines 49-55. Likewise, United States Patent No. 4,521,431 ("the '431 patent") teaches a syrup formulation or ranitidine hydrochloride. '431 patent, col. 2-3, lines 66-68.

United States Patent No. 4,585,790 ("the '790 patent") similarly discloses an aqueous formulation of ranitidine. The '790 patent further discloses formulations within the pH ranges of 6.7 to 7.3, 6.8 to 7.1, 6.5-7.5 and 7.0. The '790 patent discloses the use of buffering salts, e.g., phosphate salts. The '790 patent also discloses formulations with ranitidine concentrations in the oral formulation, expressed as free base in the ranges of 20-400 mg per 10 ml, for example 20-200 mg per 10 ml, and more particularly 150 mg per 10 ml dose. See '790 patent. The '790 patent further discloses formulations using ranitidine in the form of its hydrochloride salt. Accordingly, the '790 patent discloses each element of each of the claims of the '249 patent, with the exception of the use of ethanol to stabilize the formulation.

However, the use of ethanol to stabilize a pharmaceutical formulation is obvious. Indeed, it is widely known that ethanol is useful as a preservative in aqueous

pharmaceutical formulations. The Theory and Practice of Industrial Pharmacy (Leon Lachman, et al. eds., Lea & Febiger 1970) suggests the use of ethanol as a preservative:

> This can be done either by incorporating sufficient concentration of preservative, so that a diluted sample of the product resists microorganism growth, or by including approximately 5 to 10 per cent ethanol in the formulation.

Lachman, p. 451. Likewise, it was known that ethanol was useful in formulations for H_2 receptor antagonist drugs. The Physicians Desk Reference/Tagamet ("PDR Tagamet") also teaches ethanol as a preservative in pharmaceutical syrups for cimetidine, a H_2 receptor antagonist drug that it similar to ranitidine.

Further, two Chemical Abstracts (CA 97-61014G and CA 104-102280Z) teach the combination of ranitidine and ethanol. As noted above, during prosecution of the parent applications to the '249 patent, the claims were repeatedly rejected as being unpatentably obvious in light of two Chemical Abstracts (CA 97-61014G and CA 104-102280Z) on the basis that the abstracts taught the combination of ranitidine and ethanol. See April 29, 1988 Office Action, p. 3, United States Patent Application No. 07/131,442 and June 28, 1989 Office Action, p. 3, United States Patent Application No. 07/344,620.

As a result, the claimed combination of the ranitidine oral solution disclosed in the '790 patent with the ethanol disclosed in numerous other references, including but not necessarily limited to, Lachman, the PDR Tagamet, and the two above-referenced Chemical Abstracts was obvious. The motivation to combine these references is found in that each of them relate to ranitidine oral solutions or H_2 receptor antagonist formulations. This is further evidenced by the fact that the applicant for the '249 patent was inspired by the Tagamet solution to try adding ethanol to the ranitidine solution disclosed in the '790 patent.

In further response, Teva USA incorporates its answer to Interrogatory No. 8.

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